

1/14

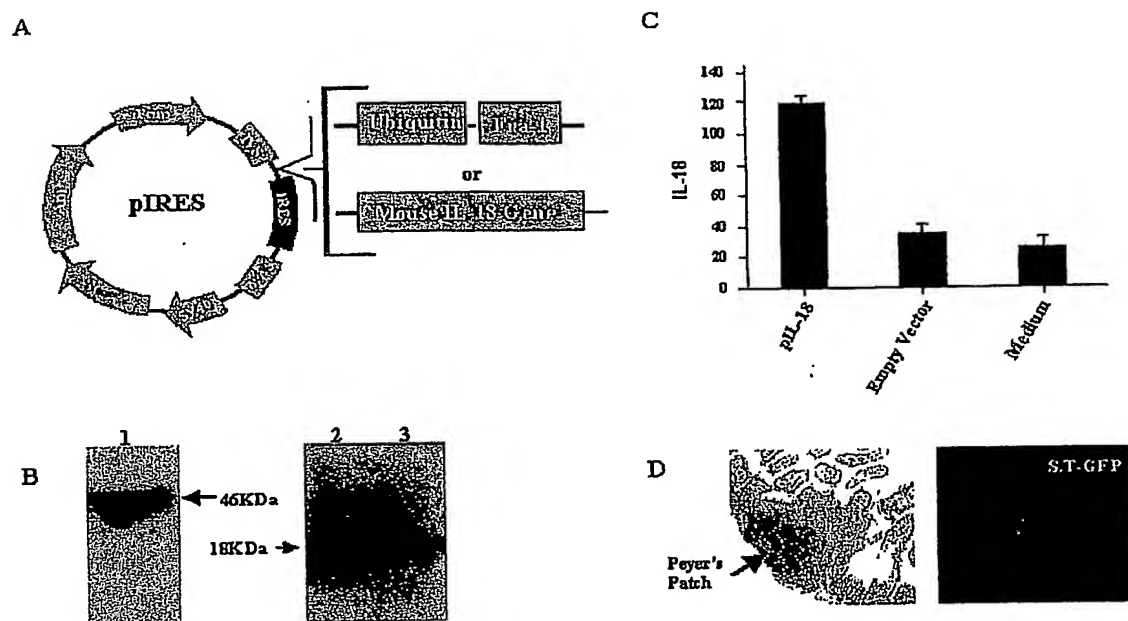


FIG. 1

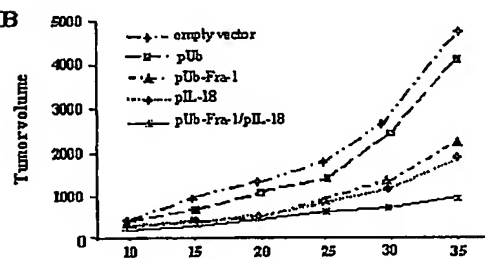
2/14

A

Suppression of lung metastases of D2F2 by oral DNA vaccine

| Treatment groups | Metastasis Score |
|---------------------|------------------|
| A. Empty vector | 2 3 3 3 3 3 3 |
| B. pUb | 3 3 3 3 3 3 3 |
| C. pUb-Fra-1 | 1 1 2 2 2 2 2 3 |
| D. pIL-18 | 0 0 1 1 1 2 2 2 |
| E. pUb-Fra-1/pIL-18 | 0 0 0 0 0 1 1 2 |

B



C

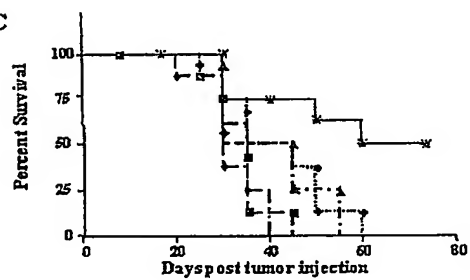


FIG. 2

3/14

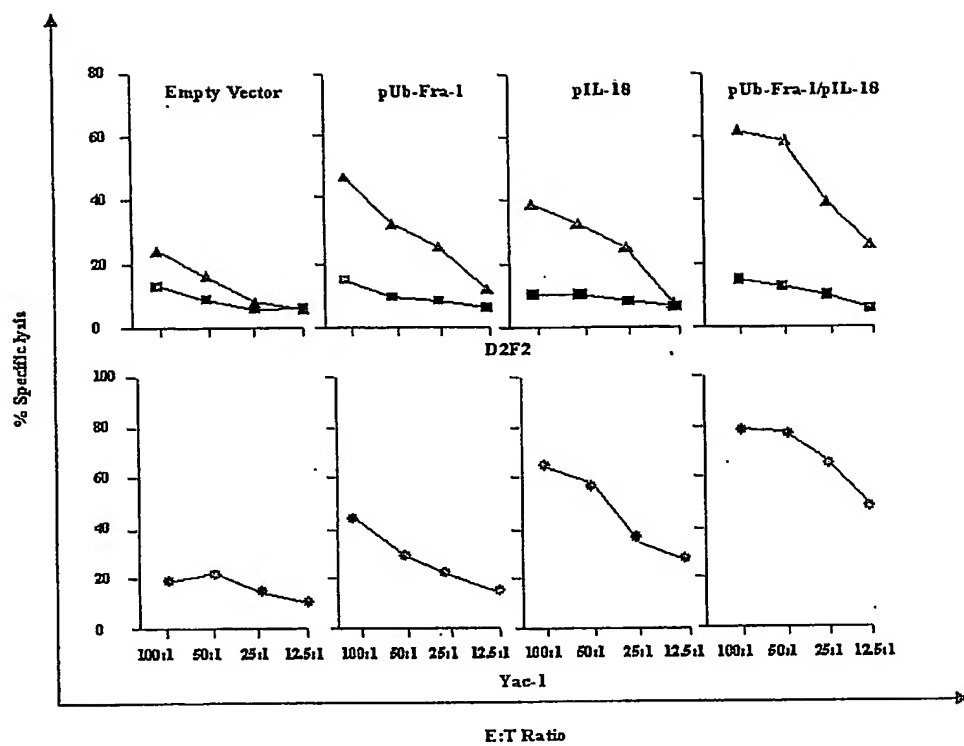


FIG. 3

4/14

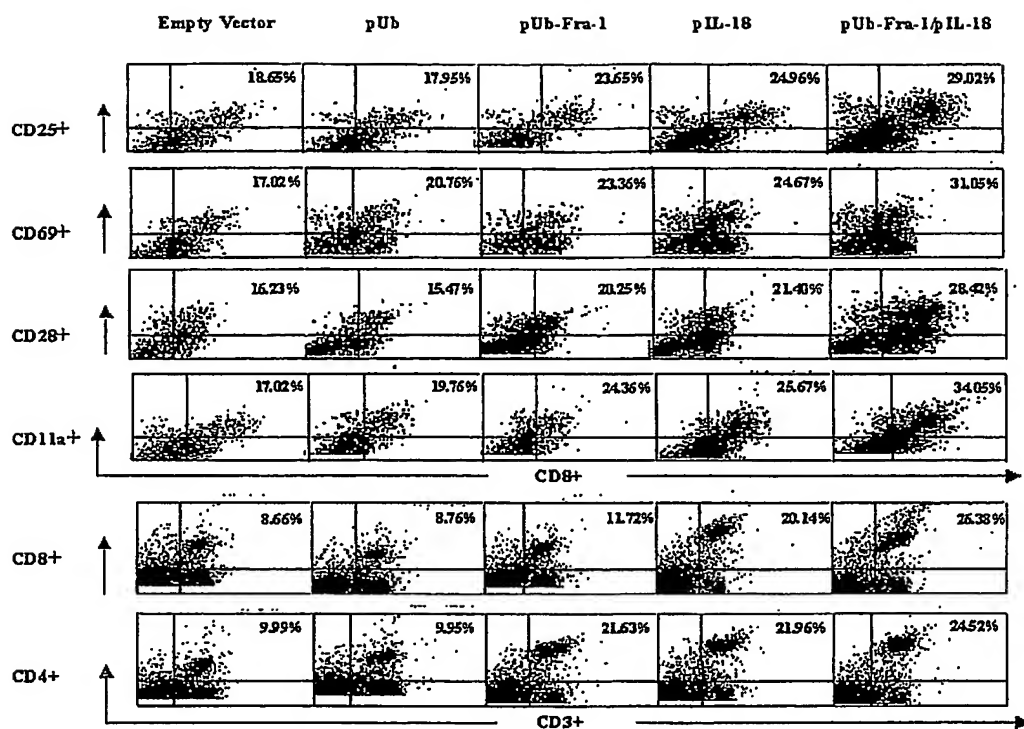


FIG. 4

5/14

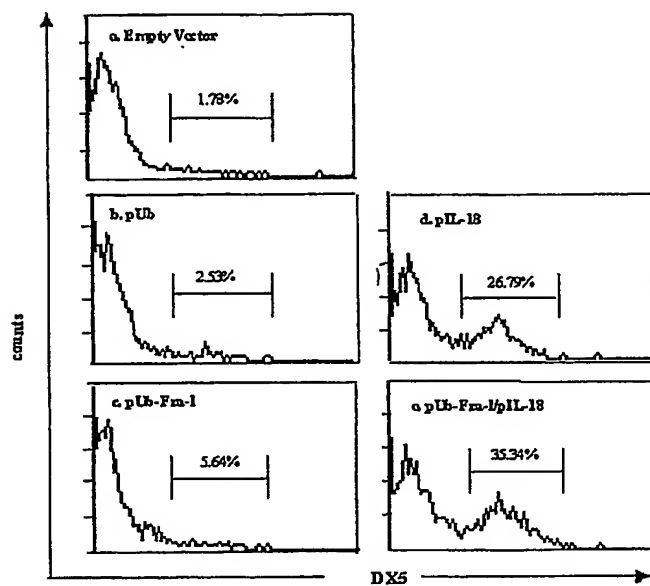


FIG. 5

6/14

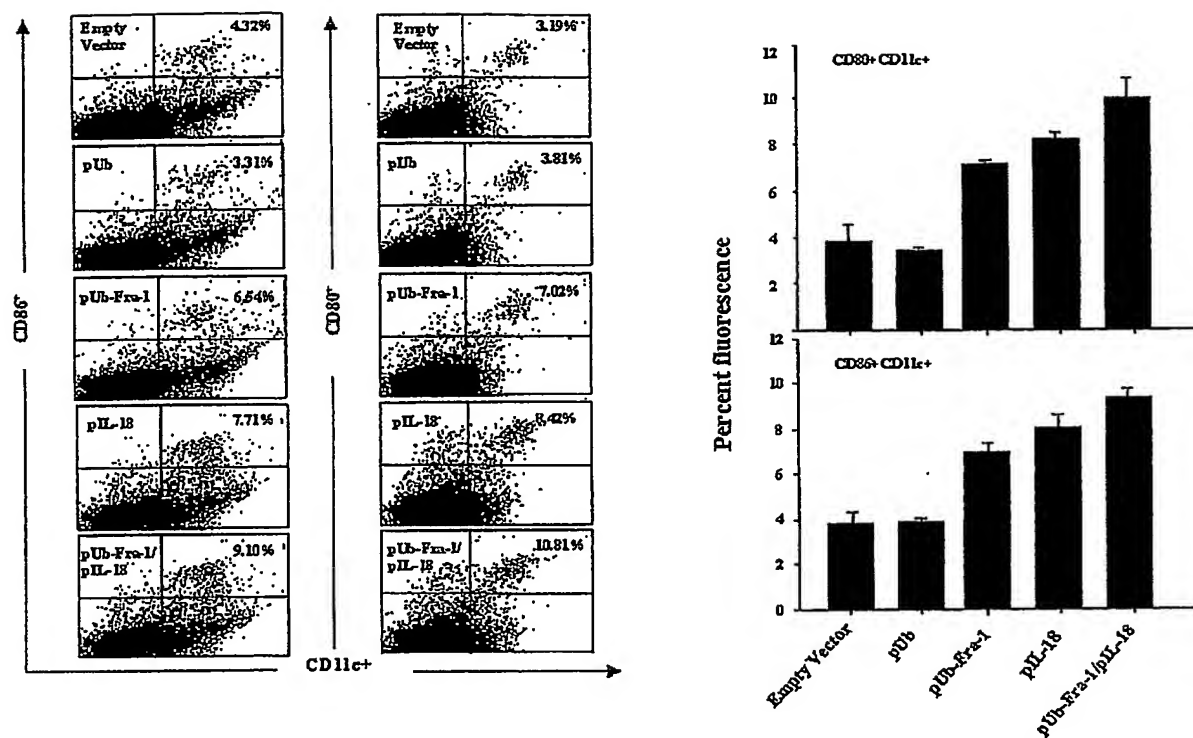


FIG. 6

7/14

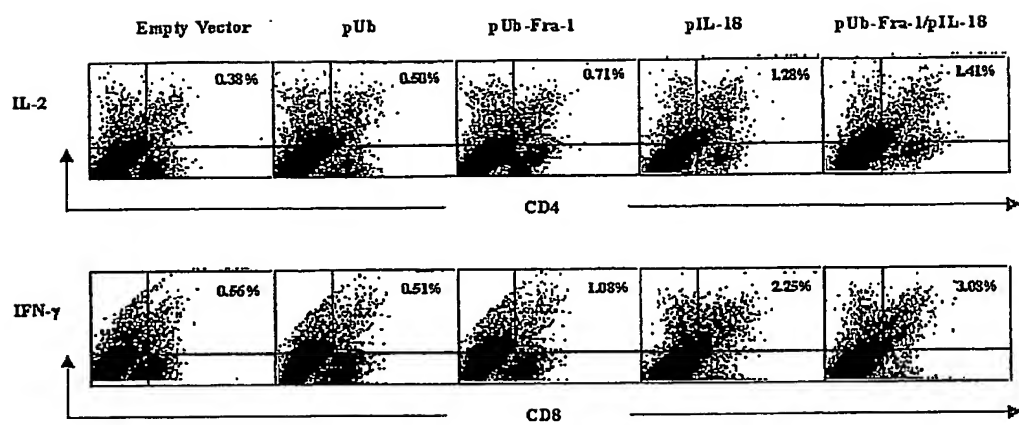


FIG. 7

8/14

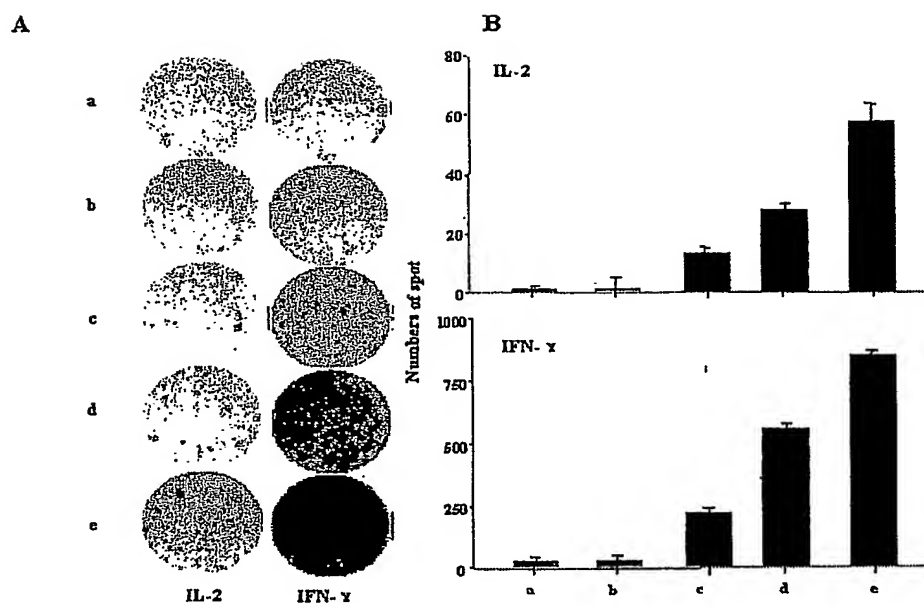


FIG. 8

9/14

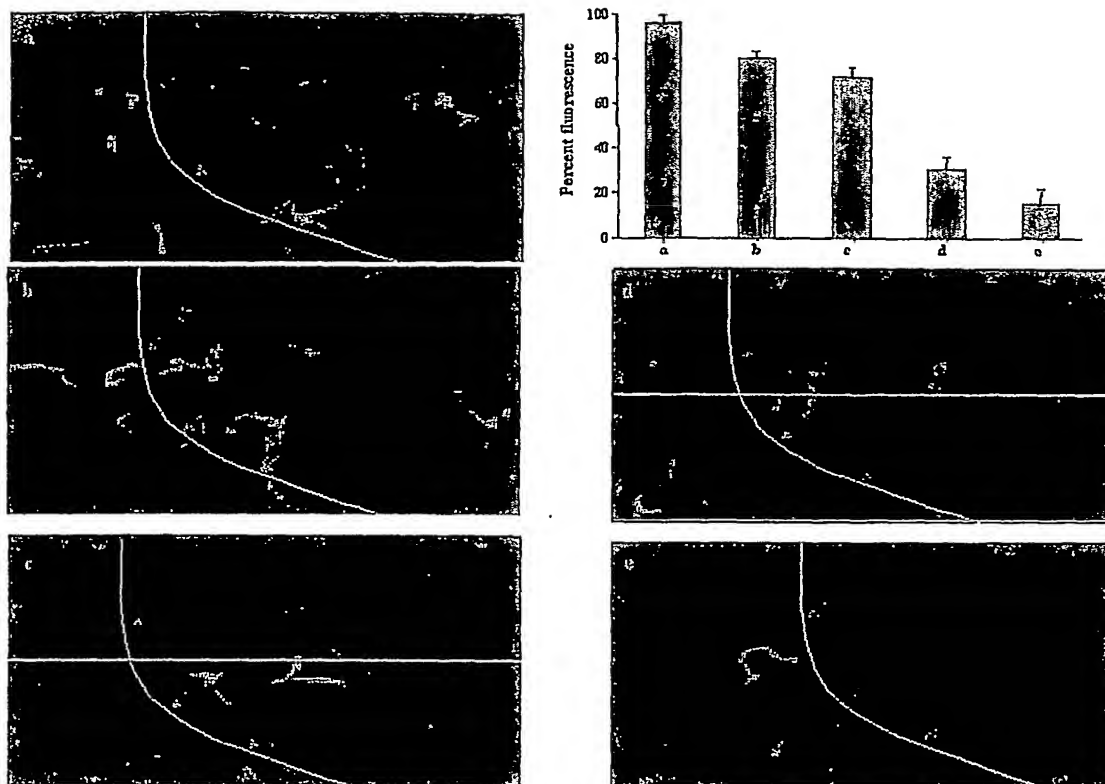


FIG. 9.

10/14

Homo sapiens - Fra-1

VERSION NM_005438.1 GI:4885242

```

1 agccgtgtac cccgcagagc cgccagcccc gggcatgttc cgagacttcg gggaaacccgg
61 cccgagctcc gggaacggcg gcgggtacgg cggcccccg cagcccccg ccgcagcgca
121 ggcagcccag cagaagttcc acctggtgcc aagcatcaac accatgagtg gcagtcagga
181 gctgcagtgg atggtacagc ctcatttcct gggggcccagc agttacccca ggcctctgac
241 ctaccctcag tacagcccc cacaaccccg gccaggagtc atccggggccc tggggccgccc
301 tccaggggta cgtcgaaggc cttgtgaaca gatcagcccg gaggaagagg agcgccgccc
361 agtaaggcgc gagcggaaca agctggctgc ggccaagtgc aggaaccgga ggaaggaaact
421 gaccgacttc ctgcaggcgg agactgacaa actggaagat gagaaatctg ggctgcagcg
481 agagattgag gagctgcaga agcagaagga gcgcctagag ctggtgctgg aagccccaccg
541 acccatctgc aaaatcccg aaggagccaa ggagggggac acaggcagta ccagtggcac
601 cagcagccca ccagccccct gccgccctgt accttgtatc tccctttccc cagggcctgt
661 gcttgaacct gaggcactgc acacccccac actcatgacc acaccctccc taactccttt
721 cacccccagc ctggtcttca cctaccccag cactcctgag ccttgtgcct cagctcatcg
781 caagagtagc agcagcagcg gagacccatc ctctgacccc cttggctctc caaccctcct
841 cgctttgtga ggcgcctgag ccctactccc tgcagatgcc accctagcca atgtctcctc
901 cccttcccc accggtccag ctggcctgga cagtatccca catccaactc cagc

```

(SEQ ID NO: 1)

Homo sapiens - Fra-1

```

MFRDFGEPGPSSSGNGGGYGGAQPPAAAQAAQKQKFLVPSINTMSGSQELQWMVQPHFLGPSSYPRPLTY
PQYSPPQPRPGVIRALGPPPGVRRRPCEQISPEEEERRRVRERENKLAALKCRNRKELTDFLQAETDKL
EDEKSGLQREIEELQKQKERLELVLEAHRPICKIPEGAKEGDTGSTSGTSSPPAPCRPVPCISLSPGPVL
EPEALHTPTLMTTPSLTPFTPSLVFTYPSTPEPCASAHKSSSSSGDPSSDPLGSPTLLAL

```

(SEQ ID NO: 2)

FIG. 10

Murine Fra-1

(DNA Sequence, SEQ ID NO: 3; Protein Sequence, SEQ ID NO: 4)

| | | |
|-----|---|-----|
| 1 | ATGTACCGAGACTACGGGGAACCGGGACCGAGCTCCGGGGCTGGCAGCGCGTACGGTTCGC | 60 |
| 1 | M Y R D Y G E P G P S S G A G S A Y G R | 20 |
| 61 | CCCGCGCAGCCCCCGCAAGCTCAGGCACAGACCGCCAGCAGCAGAAGTTCCACTTTGTG | 120 |
| 21 | P A Q P P Q A Q A Q T A Q Q Q K F H F V | 40 |
| 121 | CCAAGCATCGACAGCAGCAGCCAGGAAGTGCCTGGATGGTGCAGCCTCATTTCCTGGGA | 180 |
| 41 | P S I D S S S Q E L H W M V Q P H F L G | 60 |
| 181 | CCCACTGGCTATCCCCGACCTCTGGCCTATCCCCAGTACAGTCCCCCTCAGCCCCGGCCA | 240 |
| 61 | P T G Y P R P L A Y P Q Y S P P Q P R P | 80 |
| 241 | GGAGTCATACGAGCCCTAGGGCCACCTCCGGGGGTGCGTCGCAGGCCCTGCGAGCAGATC | 300 |
| 81 | G V I R A L G P P P G V R R R P C E Q I | 100 |
| 301 | AGCCCGAGAGGAGGAAGAGCGCCGAGGGTGAGACGCGAGCGGAACAAGCTAGCAGCTGCT | 360 |
| 101 | S P E E E E R R R V R R E R N K L A A A | 120 |
| 361 | AAGTGCAGAAACCGAAGAAAGGAGCTGACAGACTTCCTGTCAGGCGGAGACCGACAAATTG | 420 |
| 121 | K C R N R R K E L T D F L Q A E T D K L | 140 |
| 421 | GAGGATGAGAAATCGGGGCTGCAGCGAGAGATTGAAGAGCTGCAGAAGCAGAAGGAACGC | 480 |
| 141 | E D E K S G L Q R E I E E L Q K Q K E R | 160 |
| 481 | CTTGAGCTGGTGCTGGAAGCCCATCGCCTCATCTGCAAAATCCCAGAAGGAGACAAGAAG | 540 |
| 161 | L E L V L E A H R L I C K I P E G D K K | 180 |
| 541 | GACCCAGGTGGTTCTGGCAGCACCAGCGGGGCTAGCAGCCCACCAGCCCCCGGCCGCCCA | 600 |
| 181 | D P G G S G S T S G A S S P P A P G R P | 200 |
| 601 | GTGCCTTGTCATCTCCCTTTCTCCAGGACCCGTACTTGAACCGGAAGCACTGCATACCCCC | 660 |
| 201 | V P C I S L S P G P V L E P E A L H T P | 220 |
| 661 | ACGCTCATGACCACACCCTCTCTGACTCCTTTTACTCCGAGTCTGGTTTTTCACCTATCCT | 720 |
| 221 | T L M T T P S L T P F T P S L V F T Y P | 240 |
| 721 | AGCACACCAGAACCTTGCTCCTCCACTCACCGAAAGAGTAGCAGCAGCAGTGGCGACCCC | 780 |
| 241 | S T P E P C S S T H R K S S S S S G D P | 260 |
| 781 | TCCTCCGACCCCCTGGGCTCTCCTACACTCCTGGCTTTGTGA | 822 |
| 261 | S S D P L G S P T L L A L * | 274 |

FIG. 11

12/14

Homo sapiens - IL-18

VERSION NM_001562.2 GI:27502389

```
1 atttctctccc cagcttgctg agccctttgc tcccctggcg actgcctgga cagtcagcaa
61 ggaattgtct cccagtgcac ttgtccctcc tggctgccaa ctctggctgc taaagcggct
121 gccacctgct gcagtctaca cagcttcggg aagaggaaaag gaacctcaga ccttcagat
181 cgcttcctct cgcaacaaac tatttgtcgc aggaataaaag atggctgctg aaccagtaga
241 agacaattgc atcaactttg tggcaatgaa atttattgac aatacgcttt actttatagc
301 tgaagatgat gaaaacctgg aatcagatta ctttggcaag cttgaatcta aattatcagt
361 cataagaaat ttgaatgacc aagttctctt cattgaccac ggaaatcggc ctctatttga
421 agatatgact gattctgact gtagagataa tgcaccccg accatattta ttataagtat
481 gtataaagat agccagccta gaggtatggc tgtaactatc tctgtgaagt gtgagaaaat
541 ttcaactctc tcctgtgaga acaaaattat ttcctttaag gaaatgaatc ctctgataa
601 catcaaggat acaaaaagtg acatcatatt ctttcagaga agtgtcccag gacatgataa
661 taagatgcaa tttgaatctt catcatacga aggatacttt ctagcttggtg aaaaagagag
721 agaccttttt aaactcattt tgaaaaaaga ggatgaattg ggggatagat ctataatggt
781 cactgttcaa aacgaagact agctattaaa atttcatgcc gggcgagctg gctcacgcct
841 gtaatcccag ccctttggga ggctgaggcg ggcagatcac cagaggtcag gtgttcaaga
901 ccagcctgac caacatggtg aaacctcatc tctactaaaa atacaaaaaa ttagctgagt
961 gtagtgacgc atgccctcaa tcccagctac tcaagaggct gaggcaggag aatcacttgc
1021 actccggagg tagaggttgt ggtgagccga gattgcacca ttgcgctcta gcctgggcaa
1081 caacagcaaa actccatctc aaaaaataaa ataaataaat aaacaaataa aaatttcata
1141 atgtg (SEQ ID NO: 5)
```

Homo sapiens - IL-18

```
MAAEPVEDNCINFVAMKFIDNTLYFIAEDDENLESDFGKLESKLSVIRNLNDQVLFIHQGNRPLFEDMT
DSDCRDNAPRTIFIISMYKDSQPRGMAVTISVKCEKISTLSCENKIISFKEMNPPDNIKDTKSDIIFQ
SVPGHNDKMQFESSYEGYFLACEKERDLFKLILKKEDELGDRSIMFTVQNE
(SEQ ID NO: 6)
```

FIG. 12

13/14

Murine IL-18**(DNA Sequence, SEQ ID NO: 7; Protein Sequence, SEQ ID NO: 8)**

| | | |
|-----|---|-----|
| 1 | ATGGCTGCCATGTCAGAAGACTCTTGCGTCAACTTCAAGGAAATGATGTTTATTGACAAC | 60 |
| 1 | M A A M S E D S C V N F K E M M F I D N | 20 |
| 61 | ACGCTTTACTTTTATACCTGAAGAAAATGGAGACCTGGAATCAGACAACTTTGGCCGACTT | 120 |
| 21 | T L Y F I P E E N G D L E S D N F G R L | 40 |
| 121 | CACTGTACAACCGCAGTAATACGGAATATAAATGACCAAGTTCTCTTCGTTGACAAAAGA | 180 |
| 41 | H C T T A V I R N I N D Q V L F V D K R | 60 |
| 181 | CAGCCTGTGTTTCGAGGATATGACTGATATTGATCAAAGTGCCAGTGAACCCAGACCAGA | 240 |
| 61 | Q P V F E D M T D I D Q S A S E P Q T R | 80 |
| 241 | CTGATAATATACATGTACAAAGACAGTGAAGTAAGAGGACTGGCTGTGACCCTCTCTGTG | 300 |
| 81 | L I I Y M Y K D S E V R G L A V T L S V | 100 |
| 301 | AAGGATAGTAAAATGTCTACCCTCTCCTGTAAGAACAAGATCATTTCTTTGAGGAAATG | 360 |
| 101 | K D S K M S T L S C K N K I I S F E E M | 120 |
| 361 | GATCCACCTGAAAATATTGATGATATACAAAGTGATCTCATATTCTTTCAGAAACGTGTT | 420 |
| 121 | D P P E N I D D I Q S D L I F F Q K R V | 140 |
| 421 | CCAGGACACAACAAGATGGAGTTTGAATCTTCACTGTATGAAGGACACTTTCTTGCTTGC | 480 |
| 141 | P G H N K M E F E S S L Y E G H F L A C | 160 |
| 481 | CAAAGGAAGATGATGCTTTCAAACCTATTCTGAAAAAAGGATGAAAATGGGGATAAA | 540 |
| 161 | Q K E D D A F K L I L K K K D E N G D K | 180 |
| 541 | TCTGTAATGTTCACTCTCACTAACTTACATCAAAGTTAG | 579 |
| 181 | S V M F T L T N L H Q S * | 193 |

FIG. 13

14/14

Ubiquitin

(DNA Sequence, SEQ ID NO: 9; Protein Sequence, SEQ ID NO: 10)

| | | |
|-----|--|-----|
| 1 | ATGCAGATCTTCGTGAAGACCCTGACCGGCAAGACCATCACCTAGAGGTGGAGCCCAGT | 60 |
| 1 | M Q I F V K T L T G K T I T L E V E P S | 20 |
| 61 | GACACCATCGAGAACGTGAAGGCCAAGATCCAGGATAAAGAGGGCATCCCCCTGACCAG | 120 |
| 21 | D T I E N V K A K I Q D K E G I P P D Q | 40 |
| 121 | CAGAGGCTGATCTTTGCCGGCAAGCAGCTGGAAGATGGCCGCACCCTCTCTGATTACAAC | 180 |
| 41 | Q R L I F A G K Q L E D G R T L S D Y N | 60 |
| 181 | ATCCAGAAGGAGTCAACCCTGCACCTGGTCCTTCGCCTGAGAGGTGGC | 228 |
| 61 | I Q K E S T L H L V L R L R G G | 76 |

FIG. 14